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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/302,816	03/03/98	ENGELHARDT	ENZ-52(C)

EXAMINER	
ART UNIT	PAPER NUMBER
1655	8

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DATE MAILED: 04/19/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/302,816	Engelhardt et al.
Examiner	**Group Art Unit**
Arun Chakrabarti	1655

☒ Responsive to communication(s) filed on *Apr 16, 1999*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *91-149* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *91-148* is/are rejected.

☒ Claim(s) *149* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Priority

1. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 (e) as follows:

An application in which the benefits of an earlier application are desired must be copending with the prior application or with an application similarly entitled to the benefit of the filing date of the prior application.

As there is no copendency in this application, applicant is not entitled to get the priority of the parent case 08/182,621 which has been abandoned on January 13, 1994.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

3. Claims 91-96 and 99-120 are rejected under 35 U.S.C. 102 (e) as anticipated by Walker et al (U.S. Patent 5,455,166) (October 3, 1995)

Walker et al teaches an in vitro process for producing more than one copy of a specific nucleic acid, the process being independent of a requirement for the introduction of an intermediate structure for the production of the specific nucleic acid, (Abstract, Figures 1 and 2), the process comprising the steps of:

(a) providing a nucleic acid sample containing or suspected of containing the sequence of the specific nucleic acid (Example 1, column 10, lines 58-63 and Example 2, column 11, line 63 and Example 3, column 12, lines 49-53);

(b) contacting the sample with a mixture comprising:

(I) nucleic acid precursors (Figure 1)

(ii) one or more specific nucleic acid primers each of which is complementary to a distinct sequence of the specific nucleic acid (Figure 1 and Example 2, column 11, lines 56-58), and

(iii) an effective amount of a nucleic acid producing catalyst (Example 1, column 11, lines 1-7); and

c) allowing the mixture to react under isostatic conditions of temperature, buffer and ionic strength, thereby producing more than one copy of the specific nucleic acid (Figures 1 and 2 and Example 2, column 12, lines 3-6).

Walker teaches the process wherein the nucleic acid is single stranded or double-stranded DNA (Figures 1 and 2 and Examples 1 and 2).

Walker teaches the process wherein the nucleic acid is in solution (Example 2, column 11, line6 56-62).

Walker teaches the process further comprising the steps of treating the specific nucleic acid with a restriction enzyme capable of producing blunt ends (Figures 1 and 2, column 8, lines 20-60 and example 1, column 11, line 5 and example 2, column 12, line 5).

Walker teaches the process wherein the nucleic acid is isolated or purified prior to the contacting step or the reacting step (Example 3, column 12, lines 49-52).

Walker teaches the process wherein the releasing step is carried out by means of a restriction enzyme (Figures 1 and 2).

Walker teaches the process wherein the nucleic acid precursors are selected from nucleoside triphosphates and nucleoside triphosphate analogs, or a combination thereof (column 8, lines 20-60 and Example 3, column 12, line 58).

Walker teaches the process wherein the nucleic acid precursors are selected fromATP, GTP, CTP, UTP or TTP (Figures 1 and 2 and Example 2, column 12, lines 1-3).

Walker teaches the process wherein the nucleoside triphosphates analogs are naturally occurring or synthetic, or a combination thereof (Figures 1 and 2 and Example 2, column 12, lines 1-3).

Walker teaches the process wherein at least one of the nucleoside triphosphate analogs is modified on the phosphate (column 8, lines 20-60 and Example 3, column 12, line 58).

Walker teaches the process wherein the specific nucleic acid primers contains a 3'-hydroxyl group or an isosteric configuration of heteroatoms containing sulfur (Figures 1 and 2 and Example 2, column 11, lines 56-57).

Walker teaches the process wherein the specific nucleic acid primers are not substantially complementary to one another and does not contain more than five complementary to base-pairs in the sequences therein (Column 15, SEQ ID Nos; 5 and 6).

Walker teaches the process wherein the specific nucleic acid primers comprise from about 5 to 100 nucleotides (SEQ ID Nos: 4-7).

Walker teaches the process wherein the specific nucleic acid primers comprise from about 1 to 200 non complementary nucleotides (Column 15, SEQ ID Nos: 5 and 6).

Walker teaches the process wherein the nucleic acid producing catalyst is selected from DNA polymerase (Example 1, column 11, lines 1-5).

Walker teaches the process further comprising the step of detecting the product by means of incorporating into the product a labeled primer (Example 3, column 12, line 65 to column 13, line 13 and Table III).

Walker teaches the process further comprising the step of regenerating the one or more specific nucleic acid primers for additional production processes (Figures 1 and 2).

4. Claims 142, 144, 146 and 147 are rejected under 35 U.S.C. 102 (b) as anticipated by Zaichikov et al. (Bioorganicheskaia Khimia, (1988 Jan), Vol. 14 (1), 121-4).

Zaichikov et al teaches a conjugate comprising a protein-nucleic acid construct, the nucleic acid construct not coding for said protein, and which conjugate produces a nucleic acid when present in a cell (Abstract, lines 1-3).

Zaichikov et al. teaches a conjugate wherein the protein comprises an RNA polymerase or a subunit thereof (Abstract, lines 1-6).

5. Claims 142-149 are rejected under 35 U.S.C. 102 (b) as anticipated by Knorre et al. (IZV SIB OTD AKAD NAUK SSSR SER BIOL NAUK (1989), Volume 0(2), pages 98-104).

Knorre et al. teaches an in vivo process for producing a specific nucleic acid, the process comprising a protein-nucleic acid construct, the nucleic acid construct not coding for said protein, and which conjugate produces a nucleic acid when present in a cell (Abstract, lines 1-19).

Knorre et al. teaches a conjugate wherein the protein comprises an RNA polymerase or a subunit thereof (Abstract, lines 1-6) and the nucleic acid construct contains the corresponding RNA polymerase promoter (Abstract, lines 1-8).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 91-120 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walker (U.S. Patent 5,455,166) (October 3, 1995) in view of Matthews et al. (Analytical Biochemistry, (1988), Vol. 169, pages 1-25).

Walker teaches the processes of claims 91-96 and 99-120 as described above.

Walker does not teach the isolation or purification of the specific nucleic acid by means of sadwich hybridization or capture sandwich hybridization.

Matthews et al teaches the isolation or purification of the specific nucleic acid by means of sadwich hybridization or capture sandwich hybridization (Figures 9, 10, 12, 13 and 14).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute sandwich hybridization model of Matthews et al. in the method of Walker, since Matthews et al states, "The sandwich hybridization strategy is not

limited to quantitation of a nucleic acid species, but can easily be applied to detection of altered restriction sites in DNA, providing the exact mutation to be detected is known (page 16, column 1, lines 7-11)."An ordinary practitioner would have been motivated to combine the sandwich hybridization model of Matthews et al. in the method of Walker, in order to achieve the express advantages noted by Matthews et al. of a method which provides easy application to detection of altered restriction sites in DNA.

8. Claims 91-96 and 99-128 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walker (U.S. Patent 5,455,166) (October 3, 1995) in view of Romano et al. (U.S. Statutory Invention Registration Number H1,825) (December 7, 1999).

Walker teaches the processes of claims 91-96 and 99-120 as described above.

Walker does not teach primers comprising at least one ribonucleic acid segment.

Walker does not teach removing of primer-coded sequences from the product by digestion with an enzyme ribonuclease H.

Romano et al teaches primers comprising at least one ribonucleic acid segment (Abstract, Table 1 and 2).

Romano et al teaches removing of primer-coded sequences from the product by digestion with an enzyme ribonuclease H (Column 6, lines 29-41).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute RNA primer based isothermal transcription and amplification model of Romano et al. in the method of Walker, since Romano et al states, "The

purpose of applying such an assay would be to determine the presence and level of these transcripts, and to use these levels for the purpose of screening of blood donors, epidemiological studies, and in clinical practice for prognosis and /or therapeutic management (column 2, lines 46-50)."An ordinary practitioner would have been motivated to combine the RNA primer based isothermal transcription and amplification model of Romano et al. in the method of Walker, in order to achieve the express advantages noted by Romano et al. of a method which provides utilization in screening of blood donors, epidemiological studies, and in clinical practice for prognosis and /or therapeutic management.

9. Claims 91-96 , 99-120 and 129-136 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walker (U.S. Patent 5,455,166) (October 3, 1995) in view of Gerdes et al. (U.S. Patent 5,955,351) (September 21, 1999).

Walker teaches the processes of claims 91-96 and 99-120 as described above.

Walker does not teach one or more specific chemically-modified primers each of which primer is substantially complementary to a distinct sequence of the specific nucleic acid.

Walker does not teach removing of primer-coded sequences from the product by digestion with an enzyme ribonuclease H.

Gerdes et al teaches one or more specific chemically-modified primers each of which primer is substantially complementary to a distinct sequence of the specific nucleic acid (Examples 3, 4, 5, 6, 7 and 8 and SEQ ID NOs:1-13).

Gerdes et al teaches removing of primer-coded sequences from the product by digestion with an enzyme ribonuclease H (Example 4, column 10, lines 47-56).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the chemically-modified primer model of Gerdes et al. in the method of Walker, since Gerdes et al states, "The process according to the present invention is suitable for the determination of all nucleic acid target sequences. The sensitivity and accuracy of this process are improved compared to the processes currently used by those skilled in the art. The invention offers the possibility of contamination free, rapid and reliable determination of the presence of specific amplified target nucleic acid (column 4, lines 41-47)."An ordinary practitioner would have been motivated to combine chemically-modified primer model of Gerdes et al. in the method of Walker, in order to achieve the express advantages noted by Gerdes et al. of a method which provides the possibility of contamination free, rapid and reliable determination of the presence of specific amplified target nucleic acid.

10. Claims 91-96 , 99-120 and 129-141 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walker (U.S. Patent 5,455,166) (October 3, 1995)in view of Gerdes et al. (U.S. Patent 5,955,351) (September 21, 1999) further in view of Courey et al. (Journal of Molecular Biology, (1988), Vol. 202, pages 35-43).

Walker in view of Gerdes et al. teach the processes of claims 91-96, 99-120 and 129-136 as described above.

Walker in view of Gerdes et al. do not teach one or more specific unmodified primers each of which primer comprises at least one non-complementary sequence to a distinct sequence of the specific nucleic acid such that upon hybridization to the specific nucleic acid at least one loop structure is formed.

Courey et al teaches one or more specific unmodified primers each of which primer comprises at least one non-complementary sequence to a distinct sequence of the specific nucleic acid such that upon hybridization to the specific nucleic acid at least one loop structure is formed (Figures 2, 5 and 6).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the loop forming supercoiling model of Courey et al. in the method of Walker, since Walker states, "The invention further relates to methods of generating amplified products which can function as probes or templates for sequence analysis (column 4, lines 41-47)." Courey et al provides further motivation as he states, "Lengths of cruciform arms are strongly dependent on sequence imperfections in the palindrome (page 36, column 1, lines 11-14)." An ordinary practitioner would have been motivated to combine the loop forming supercoiling model of Courey et al. in the method of Walker, in order to achieve the express advantages noted by Courey et al. of a method which provides the detection of sequence imperfections in a nucleic acid sample.

Allowable Subject Matter

11. Claim 149 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located In Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published In the Official Gazette, 1096 OG 30 (November 15, 1989).

Arun Kr. Chakrabarti

Arun Chakrabarti

Patent Examiner

Art Unit 1655

FEB 16 2000

JEFFREY FREDMAN
PRIMARY EXAMINER